

Validation test (“ReceptIVFity-test”) to predict the chance of pregnancy with IVF or IVF-ICSI treatment based on bacteria composition

Submission date 17/08/2018	Recruitment status No longer recruiting	☐ Prospectively registered ☒ Protocol
Registration date 30/08/2018	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 06/09/2023	Condition category Pregnancy and Childbirth	☐ Individual participant data

Plain English summary of protocol

Background and study aims

In the last decade, research has shown that microorganisms may have an impact on the outcome of assisted reproductive procedures such as IVF or IVF-ICSI. Microorganisms, together with their genetic information and the environment in which they live and interact is called the microbiome. One common type of bacteria that lives in the vagina is Lactobacillus. Studies have shown that the presence of Lactobacillus during assisted reproductive procedures can have a positive impact on the outcome. However, using the microbiome as a way of predicting the outcome of these procedures has not yet been investigated. This study aims to develop a method of using the microbiome to identify women with low, mid and high chances of becoming pregnant prior to the start of IVF or IVF-ICSI treatment. Having the ability to predict this may help couples to make decisions about whether to continue these treatments.

Who can participate?

Females aged 20-44 with a male partner, who have been indicated for IVF or IVF-ICSI

What does the study involve?

Participants will be asked to

Participants will receive a sampling protocol and collect a vaginal swab and urine sample by themselves in the IVF centre. The swab and the urine sample will take place once and have to be taken within the two months prior to the embryo transfer.

The urine sample collection will be obtained according to a standard ‘clean catch’ protocol, including washing hands thoroughly, cleaning the urinary opening with towelettes and collecting a midstream specimen in a sterile container. Vaginal samples will be taken with FLOQSwabs™. The participants will be instructed to insert the swab 3-5 centimetres beyond the vaginal orifice, and move the swab around along the vaginal wall for 10-15 seconds.

What are the possible benefits and risks of participating?

This research may not directly benefit the participants, since the test result is not shared with the participants during the study. However, the participants may help us to develop a predictive test based on the urogenital microbiome and hopefully this will contribute to a personalised

medicine approach in the future. There are no known risks to participants taking part in this study.

Where is the study run from?

Division Reproductive Endocrinology and Infertility, Department Obstetrics and Gynaecology, Erasmus University Medical Centre, Rotterdam (The Netherlands) (lead centre) and 7 other centres in The Netherlands

When is the study starting and how long is it expected to run for?

July 2014 to December 2018

Who is funding this study?

1. NGI Pre-Seed (The Netherlands)
2. RedMedTech (The Netherlands)
3. STW (The Netherlands)
4. Eurostars VALBIOME (Belgium)

Who is the main contact?

Dr Rivka Koedooder

r.koedooder@erasmusmc.nl

Contact information

Type(s)

Scientific

Contact name

Miss Rivka Koedooder

ORCID ID

<https://orcid.org/0000-0002-0233-6312>

Contact details

Dr. Molewaterplein 40

Rotterdam

Netherlands

3015 CD

Additional identifiers

Protocol serial number

METC 2014-455

Study information

Scientific Title

Analysis of the microbiome to determine the predictive accuracy of the urogenital microbiome for IVF/IVF-ICSI outcome prediction in IVF/IVF-ICSI patients

Acronym

Study objectives

The urogenital microbiome can be used as predictor for IVF/IVF-ICSI outcome.

Ethics approval required

Old ethics approval format

Ethics approval(s)

The protocol was approved by the Institutional Medical Ethical Review Board of all participating centres, the coordinating centre was Erasmus University Medical Centre, Rotterdam, The Netherlands (MEC-2014-455). Date of approval: 15/08/2014

Primary study design

Observational

Study design

Observational prospective multi-centre cohort study

Study type(s)

Diagnostic

Health condition(s) or problem(s) studied

In vitro fertilisation (IVF) and intracytoplasmic sperm injection (IVF-ICSI)

Interventions

A microbiome profiling intervention based on a urinary sample and a vaginal swab obtained prior to the start of the IVF or IVF/ICSI treatment. The ultimate goal will be to develop a predictive algorithm that enables identification of the group of women with a low, mid and high chance to become pregnant prior to the start of the IVF or IVF-ICSI treatment. Predictive knowledge of the microbiome profile may enable couples to make a more substantiated decision on whether to continue treatment or not. Hence, the unnecessary physical and emotional burden of a failed IVF or IVF-ICSI treatment can be avoided.

Participants will receive a sampling protocol and collect the samples by themselves in the IVF centre.

The urine sample collection will be obtained according to a standard 'clean catch' protocol, including washing hands thoroughly, cleaning the urinary opening with towelettes and collecting a midstream specimen in a sterile container. Vaginal samples will be taken with FLOQSwabs™.

The participants will be instructed to insert the swab 3-5 centimetres beyond the vaginal orifice, and move the swab around along the vaginal wall for 10-15 seconds.

The sampling will take place once and the swab and the urine sample have to be taken within the 2 months prior to the embryo transfer.

Intervention Type

Procedure/Surgery

Primary outcome(s)

To assess the specificity and sensitivity of the urinary and vaginal microbiome composition for the prediction of embryo implantation failure of a consecutive IVF or IVF-ICSI procedure.

1. The composition of the urinary and vaginal samples, assessed by Next Generation Sequencing and the IS-pro technique within the 2 months prior to the embryo transfer

2. Ongoing pregnancy (defined as an intrauterine embryo/foetus with detection of cardiac activity on transvaginal ultrasound between 7-9 weeks of gestation after fresh embryo transfer)
3. Sensitivity - the proportion of women who become pregnant who test mid or high chance to become pregnant based on microbiome analysis using urinary and vaginal samples (true positive (TP) / (TP + false negative (FN)))
4. Specificity - the proportion of women who do not become pregnant who test low chance to become pregnant based on microbiome analysis using urinary and vaginal samples (true negative (TN) / (TN + false positive (FP)))

Key secondary outcome(s)

There are no secondary outcome measures

Completion date

01/12/2018

Eligibility

Key inclusion criteria

1. Female
2. Indication for an IVF or IVF-ICSI procedure
3. Aged 20-44 years
4. Willing to provide a urine sample and a vaginal swab
5. Willing to provide informed consent
6. Male partner

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

20 Years

Upper age limit

44 Years

Sex

Female

Total final enrolment

192

Key exclusion criteria

1. No transferable embryos after IVF or IVF-ICSI
2. Indication for emergency IVF because of cancer or other reasons
3. AFS (American Fertility Society) III/IV classified endometriosis and pre-treatment with a GnRH

(gonadotropin-releasing hormone) analogue

4. >3 weeks use of hormonal contraceptives 3 months prior to start IVF or IVF-ICSI

5. Pregnant previously to the start of the IVF or IVF-ICSI (including miscarriage)

6. Hormonal treatments 3 months prior to start IVF or IVF-ICSI

7. Use of sperm donation

Date of first enrolment

02/06/2015

Date of final enrolment

09/04/2016

Locations

Countries of recruitment

Netherlands

Study participating centre

Erasmus University Medical Centre

Division of Reproductive Medicine

Department of Obstetrics and Gynaecology

Erasmus University Medical Centre

Wytemaweg 80

Rotterdam

Netherlands

3015 CN

Study participating centre

Radboud University Medical Centre

Division of Reproductive Medicine

Department of Obstetrics and Gynaecology

Geert Grooteplein Zuid 10

Nijmegen

Netherlands

6525 GA

Study participating centre

Isala Kliniek

Isala Voortplantingscentrum

Dokter Spanjaardweg 29

Zwolle

Netherlands

8025 BT

Study participating centre

VU University Medical Centre

Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
De Boelelaan 1117
Amsterdam
Netherlands
1081 HV

Study participating centre

Sint Elisabeth Ziekenhuis

Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
Hilvarenbeekseweg 60
Tilburg
Netherlands
5022 GC

Study participating centre

VivaNeo Medisch Centrum Kinderwens

Simon Smitweg 16
Leiderdorp
Netherlands
2353 GA

Study participating centre

University Medical Centre Utrecht

Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
Heidelberglaan 100
Utrecht
Netherlands
3584 CX

Study participating centre

Maastricht Universitair Medisch Centrum+

Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
P. Debyelaan 25
Maastricht
Netherlands
6229 HX

Sponsor information

Organisation

Erasmus University Medical Centre

ROR

<https://ror.org/018906e22>

Funder(s)

Funder type

Not defined

Funder Name

Netherlands Genomics Initiative

Funder Name

RedMedTech

Funder Name

Stichting voor de Technische Wetenschappen

Alternative Name(s)

Technology Foundation STW, Technologiestichting STW, Dutch Technology Foundation, Dutch Technology Foundation STW, STW

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

Netherlands

Funder Name

Eurostars

Alternative Name(s)

EUREKA Eurostars

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Belgium

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from r.koedooder@erasmusmc.nl. This will contain anonymised data after our primary data are published, but only if formally requested so we can control the nature of the analyses.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	04/06/2019	17/07/2020	Yes	No
Protocol article		07/12/2018	06/09/2023	Yes	No